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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/068,377	05/08/99	LASKY	L P1066P2

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1642	14

DATE MAILED: 11/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/068,377	Applicant(s) LASKY ET AL.	
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 19-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *15-18 and 22* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 5/8/99 is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

1. The Election filed August 11, 2000 (Paper No. 12) in response to the Office Action of July 5, 2000, the Amendment filed on April 11, 2000 (Paper No. 8), and the Amendment filed on October 20, 2000 (Paper No. 14) in response to the interview of October 20, 2000 (Paper No. 13) are acknowledged and have been entered.

Claims 1-22 are pending in the application. Claims 1-14 and 19-21 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to nonelected claims, as per Applicants' response, dated April 7, 2000, to the Office Action mailed on March 8, 2000. Claims 15 and 22 have been amended. Claims 15-18 and 22 are currently under prosecution.

2. Applicants' Election with traverse of Group I, claims 15-18 in Paper No. 12 is acknowledged. The traversal is on the ground(s) that it is impossible to determine whether an antibody binding to a protein represented by one linear sequence of amino acids would bind to another protein represented by another linear sequence of amino acids, even if the proteins share some sequence identity. It is acknowledged that the protein sequence cited by the examiner in the Office Action mailed July 5, 2000 (Paper No. 11) is different enough that it cannot be known that the antibody against said protein will bind the polypeptide comprising SEQ ID NO:1. The grounds for the traversal are found persuasive and the restriction requirement is withdrawn.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

(a) The oath or declaration claims benefit under 35 USC § 120 of an application (serial no. 08/938,829), which is entitled differently than the pending application (serial no. 09/068,377). Further, there is no common inventor listed in serial no. 08/938,829.

(b) The oath or declaration claims the benefit of a provisional application, serial no. 60/104589 under 35 USC § 120. A claim for the benefit of a provisional application's filing date must be made under 35 USC § 119(e).

Specification

4. The specification on page 1 must be amended to reflect the priority claimed in the declaration.

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 15-18 and 22 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The utility of an antibody to a specific protein, such as PSTPIP, is dependent upon the utility of the protein to which it binds. The asserted utilities for a PSTPIP polypeptide include their use in "a variety of indications wherein the skilled artisan wishes to induce the polymerization of actin monomers" (page 34, lines 38-39), their use as "molecular markers of the tissues in which they are expressed" (page 35, line 2), their use as "protein molecular weight markers on protein gels" (page 35, lines 4-5), their use in "*in vitro* assays, together with PTP HSCF, to identify inhibitors of the PTP-PSTPIP interaction" (page 35, lines 13-14), and "mutants (amino acid sequence variants) of native PSTPIP polypeptides can be used in vivo in transfected recombinant host cells to identify other components of the cell divisional machinery" (page 35, lines 19-20), for example, in yeast two-hybrid system assays. The specification also discloses an asserted utility for an antibodies capable of specific binding to PSTPIP polypeptides, per se, which is "to identify rapidly dividing cells, which, in turn are used to image tumors comprised of such rapidly dividing cells" (page 35, lines 23-24).

The specification teaches that a function of a PSTPIP polypeptide is to interact with a protein tyrosine phosphatase (PTP), and more specifically, to act as a substrate for a PTP as it is dephosphorylated (page 2, line 16). However, neither the specification nor the art of record teach a

specific biological function of mouse PSTPIP or of any homologue of mouse PSTPIP, beyond disclosing that PSTPIP binds to and acts as a substrate for PTP. The specification discloses that "one role that PSTPIP **might** [emphasis added] play in the cleavage of furrow is the reorganization of polymerized actin" (page 43, line 10). Further, the specification discloses that the results of Example 5 "suggest that the unregulated expression of PSTPIP in vivo results in the induction of extended filopodial-like structures, consistent with the **possibility** [emphasis added] that the protein may induce an inappropriate polymerization of the cortical cytoskeleton" (page 43, lines 27-29). Clearly, this recitation and others in the specification imply that PSTPIP polypeptides "are associated with the polymerization of actin monomers" (page 1, lines 4-7), but the specification also teaches that PSTPIP does not act alone. Rather it seems that PSTPIP acts in concert with a number of other proteins to transmit signals that regulate diverse biological activities, including but not limited to actin monomer polymerization, but via physiological mechanisms that are not understood (page 1, line 13).

Although, the specification teaches that PSTPIP is associated with actin polymerization, it cannot be determined how or in what context a PSTPIP polypeptide might be able to induce the polymerization of actin monomers; nor, can it be determined how this ability is to be monitored in the presence of an agonist or antagonist. The specification does not teach that PSTPIP is capable of interacting or binding to actin monomers directly; and it does not teach that PSTPIP is able to directly catalyze actin polymerization. Moreover, in view of disclosures in the specification set

forth above, it is clear that PSTPIP does not act in isolation to catalyze or even to induce another protein to catalyze the polymerization of actin monomers. Rather, it seems that PSTPIP is a component of a cascade of signaling events that is mediated by a wide variety of proteins with distinct functions (see pages 1-2). In the absence of evidence of any specific biological function, for example that PSTPIP is able to induce the polymerization of actin monomers in isolation of other components of the regulatory signaling cascade, one of skill in the art cannot predict that a PSTPIP polypeptide will have the ability to do so. Since the specific *biological* function of mouse PSTPIP is not disclosed in the specification or in the art, it is impossible to establish a specific and substantial asserted utility. Therefore, it is not possible to establish a specific or substantial utility for an antibody capable of specific binding to a PSTPIP polypeptide.

The asserted utility of variants or homologues of PSTPIP is based upon a presumption that mouse PSTPIP has the prescribed biological function disclosed in the specification. However, as set forth above, the specification has not provided sufficient evidence that mouse PSTPIP is capable of either catalyzing the polymerization of actin monomers or inducing the polymerization of actin monomers in concert with other proteins. As set forth above, Applicants' presumption that mouse PSTPIP has the specific biological function of inducing actin polymerization is based upon an implied association supported by observations that PSTPIP, when over-expressed in a cell, co-localizes with polymerized actin fibers (see Example 5, page 43). Nonetheless, because of sequence differences inherent to a variant or homologue of mouse PSTPIP, one of skill in the art

cannot predict, based upon sequence homology alone, that said variant or homologue will have the same activity as that protein to which is being compared for the following reasons:

One skilled in the relevant art cannot accurately predict the effects of the dissimilarities in the sequences identified in SEQ ID NO:1 and of putatively related family members upon protein structure and function. Bowie, et al (*Science*, 1990, **257**: 1306-10) taught that an amino acid sequence encodes a message that determines the shape and function of a protein; and, that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome. The cited reference also taught that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (page 1306, column 1). Bowie, et al taught that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship and these regions can tolerate only conservative substitutions or none at all (page 1306, column 2). The sensitivity of proteins to alterations of even a single amino acid in a sequence is exemplified by Burgess, et al (*Journal of Cell Biology*, 1990, **111**: 2129-2138). This reference taught that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding

and biological activity of the protein. Lazar, et al (*Molecular and Cellular Biology*, 1988, **8**: 1247-1252) taught that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect but that a replacement with serine or glutamic acid sharply reduced its biological activity. These references (Burgess, et al and Lazar, et al) demonstrated that even a single amino acid substitution could often dramatically effect the biological activity and the structure-function characteristics of a protein. Thus, in light of the disclosed invention, the function of the PSTPIP polypeptides encoded by nucleic acid molecules that hybridize to the complement of the polypeptide sequence indicated by SEQ ID NO:2 cannot be predicted based upon sequence similarity with SEQ ID NO:1; and, nor would one of skill in the art expect the function to be the same as that of mouse PSTPIP. Therefore, it is impossible to establish a specific and substantial asserted utility for amino acid sequence variants or other mammalian homologues of mouse PSTPIP, since the specific biological function of said variants and homologues can not be predicted based upon sequence similarity alone.

The asserted utilities for PSTPIP polypeptides lack specificity since they are generally applied to many unrelated polypeptides. For example, any polypeptide having a known molecular weight can be used by one of skill in the art as a protein molecular weight marker on protein gels. Likewise, any polypeptide can be used by one of skill in the art as a molecular marker of the tissues in which they are expressed. The other asserted utilities of PSTPIP polypeptides, which include their use in different assays, could also be generally applied to any polypeptide known

to interact directly with other proteins to mediate a specific biological response, such as a protein phosphatase that binds to and dephosphorylates a protein substrate. Moreover, the latter asserted utilities are aptly considered to be invitations to one of skill in the art to experiment with PSTPIP polypeptides; and therefore, are not considered to be specific to PSTPIP polypeptides.

The asserted utility for an antibody capable of specific binding to a PSTPIP polypeptide, per se, lacks specificity since it is generally applied to many unrelated antibodies. An antibody to any other protein that is expressed in dividing cells could be used in this instance; an antibody to cyclin A, for example, is commonly used to identify cycling cells and could be used to image tumors comprising actively dividing cells. Therefore, the asserted utilities are not considered "specific" utilities; i.e. they are not specific to an antibody capable of specific binding to a PSTPIP polypeptide. Moreover, since the asserted utilities of PSTPIP polypeptides are neither specific nor well established, the utility of an antibody capable of specific binding to PSTPIP is not considered specific or well established.

Because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility cannot be assessed.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 15-18 and 22 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. If Applicant were able to overcome the 35 USC § 101 and the 35 USC § 112, first paragraph rejections above, claim 22 would still be rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 22 recites a method for using an antibody capable of specifically binding PSTPIP and identifying said antibody as either an agonist or an antagonist of PSTPIP, comprising contacting PSTPIP with said antibody and monitoring the ability of PSTPIP to induce the polymerization of actin monomers.

The specification teaches that PSTPIP is localized to the cytoplasm or interior of the cell (see Example 4, page 42). The specification teaches that "antibodies exhibit binding specificity to a specific antigen" (page 10, line 15). The specification teaches that an agonist or antagonist is an antibody capable of specifically binding PSTPIP, and which upon binding PSTPIP either stimulates or inhibits the biological function of PSTPIP, respectively (page 8, line 29-38). The specification teaches that the

biological function of a PSTPIP polypeptide is to interact with a protein tyrosine phosphatase (PTP), and more specifically, to act as a substrate for a PTP as it is dephosphorylated (page 2, line 16). The specification teaches that a whole family of PTPs "function to modulate the positive or negative signals induced by various protein tyrosine kinases" (page 1, line 17). Further, the specification teaches that the biological function of PTPs "are mediated through their interaction with critical cytoplasmic signaling proteins involved with the transmission of information from various cell surface receptors" (page 2, lines 13-15). Example 5 teaches that PSTPIP co-localizes with actin stress fibers at the cortical surface of the interior of a cell (page 43, lines 16-17) and that over-expression of PSTPIP within the cell correlates to a morphological change to the cell that is characterized by the appearance filopodial-like structures filled with polymerized actin (page 43, lines 18-20). Clearly, this recitation and others in the specification imply that PSTPIP polypeptides "are associated with the polymerization of actin monomers" (page 1, lines 4-7), but the specification also teaches that PSTPIP does not act alone. Rather it seems that PSTPIP acts in concert with a number of other proteins to transmit signals that regulate diverse biological activities, including but not limited to actin monomer polymerization, but via physiological mechanisms that are not understood (page 1, line 13).

One cannot extrapolate the teachings of the specification to the enablement of the claims for the following reasons. The specification does not teach any specific biological function of a PSTPIP polypeptide, except binding to a protein tyrosine phosphatase. Although, the specification

teaches that PSTPIP is associated with actin polymerization, it cannot be determined how or in what context a PSTPIP polypeptide might be able to induce the polymerization of actin monomers; nor, can it be determined how this ability is to be monitored in the presence of an agonist or antagonist. The specification does not teach that PSTPIP is capable of interacting or binding to actin monomers directly; and it does not teach that PSTPIP is able to directly catalyze actin polymerization. Moreover, in view of disclosures in the specification set forth above, it is clear that PSTPIP does not act in isolation to catalyze or even to induce another protein to catalyze the polymerization of actin monomers. Rather, it seems that PSTPIP is a component of a cascade of signaling events that is mediated by a wide variety of proteins with distinct functions (see pages 1-2). In the absence of evidence of any specific biological function, for example that PSTPIP is able to induce the polymerization of actin monomers in isolation of other components of the regulatory signaling cascade, one of skill in the art cannot predict that a PSTPIP polypeptide will have the ability to do so. Therefore, one cannot use the invention, as claimed, to identify an agonist or an antagonist of the ability to induce polymerization of actin monomers.

Furthermore, the specification teaches that PSTPIP is an intracellular protein. In order to practice the invention as claimed, the integrity of a cell membrane would necessarily have to be disrupted in order to contact PSTPIP with an antibody; and one would not expect PSTPIP to function normally is a disrupted, non-viable cell. As such, the specification does not teach one how to make or use the method of identifying an agonist or an antagonist antibody.

In consideration of the above, one would be forced into undue experimentation to practice the claimed invention.

11. If Applicant were to overcome the 35 USC § 101 and the 35 USC § 112, first paragraph rejections above, claims 15-18 and 22 would still be rejected under 35 USC § 112, first paragraph, because the specification, while being enabling for an antibody capable of specific binding to a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 and an assay method for using said antibody to identify an agonist or an antagonist of PSTPIP activity, does not reasonably provide enablement for claims drawn to an antibody capable of specific binding to a PSTPIP polypeptide comprising the amino acid sequence encoded by a nucleic acid which hybridizes under specifically claimed stringent conditions to the complement of the nucleic acid molecule comprising the polynucleotide sequence indicated by SEQ ID NO:2 or an assay method using said antibody to identify an agonist or an antagonist of PSTPIP activity. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Claims 15-18 are drawn to an antibody and a hybridoma producing said antibody, wherein the antibody is capable of specifically binding a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule which is capable of hybridizing under specifically claimed stringent conditions to the complement of the nucleic acid molecule comprising the polynucleotide sequence indicated by SEQ ID NO:2. Claim

22 is drawn to a method of using said antibody in order to identify said antibody as either an agonist or an antagonist. When given the broadest, reasonable interpretation, the claims are clearly intended to encompass antibodies capable of specifically binding a whole universe of polypeptides encoded by the genus of nucleic acid molecules that are at least partially complementary to the polynucleotide sequence indicated by SEQ ID NO:2.

The specification teaches the polynucleotide sequence of a cDNA (SEQ ID NO:2), which encodes a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1. The specification teaches that there are multiple sets of parameters and conditions one may employ for performing a stringent hybridization analysis (page 13, line 30 to page 14, line 2). However, none of these parameters are limiting. The specification teaches that "antibodies exhibit binding specificity to a specific antigen" (page 10, line 15). The specification teaches that an agonist or antagonist is an antibody capable of specifically binding PSTPIP, and which upon binding PSTPIP either stimulates or inhibits the biological function of PSTPIP, respectively (page 8, line 29-38).

One cannot extrapolate the teachings of the specification to the scope of the claims for the following reasons. Claims 15 and 22 specifically recite a set of stringent hybridization conditions. However, it is noted that no wash step(s) or conditions for such were recited in these claims. One skilled in the art would expect that at the hybridization temperature claimed in the absence of a wash step(s), a whole universe of complementary nucleic acid molecules would hybridize, many of which would encode polypeptides that share neither structure nor function with PSTPIP. Claims

15 and 22 recite that the antibody is capable of binding a polypeptide encoded by a hybridizing nucleic acid molecule, which "substantially retains the ability to bind a protein tyrosine phosphatase". However, the meaning of the language "*substantially* retaining the ability to bind" recited in both claims cannot be ascertained for the reasons set forth below. Thus, the claims are interpreted to encompass a genus of polypeptides encoded by a multitude of polypeptides, said polypeptides having a ranging retention of ability to bind a protein tyrosine phosphatase (PTP), wherein the ability retained by said polypeptides ranges from no retention to full retention of the ability to bind PTP. The specification does not teach how to use the broadly claimed polypeptides encompassed by the claims.

The specification provides insufficient guidance with regard to these issues and provides no working examples that would provide guidance to one skilled in the art on how to use the broadly claimed genus. For the above reasons, undue experimentation would be required to practice the claimed invention.

12. In the event Applicant were able to overcome the 35 USC § 112, first paragraph rejection above, claims 15-18 and 22 would still be rejected under 35 USC § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention.

The written description in this case only set forth the amino acid sequence of PSTPIP in SEQ ID NO:1, which is encoded by the

polynucleotide sequence indicated by SEQ ID NO:2, and the sequence of a human homologue of mouse PSTPIP (SEQ ID NO:29) and therefore, the written description is not commensurate in scope with an antibody capable of specific binding to a polypeptide encoded by a nucleic acid molecule that hybridizes under specifically claimed stringent conditions to the complement of the polynucleotide indicated by SEQ ID NO:2.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath*, page 1116).

The specification teaches the sequence of a mouse cDNA clone (SEQ ID NO:2) that encodes PSTPIP comprising the amino acid sequence indicated by SEQ ID NO:1. The specification also teaches the sequence of nucleic acid molecule encoding a human homologue of mouse PSTPIP (SEQ ID NO:28). On page 7, lines 24-27, Applicant recites the following:

> Such PSTPIP homologues may be identified in such mammals, for example, human, rabbit, rat, porcine, non-human primates, equine, and ovine. Screening cDNA libraries prepared from these mammals with a probe derived from the nucleic acid encoding the murine PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO:1) will allow identification of such homologues.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it.

The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera . A description of a genus of hybridizing polynucleotides may be acheived by means of a recitation of a representative number of hybridizing polynucleotides, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural freatures common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient

descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. The specification proposes to discover other members of the genus by using hybridization. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore, only an antibody capable of specific binding to a polypeptide encoded by a nucleic acid molecule comprising the polynucleotide sequence indicated by SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 15-18 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15-18 and 22 are indefinite because claims 15 and 22 recite the term "substantially". The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Sodhi, et al (*Biochemistry and Molecular Biology International*, 1995, **35**: 559-565; see abstract).

Claims 15-16 are drawn to an antibody capable of specifically binding a PSTPIP polypeptide comprising the amino acid sequence indicated by

SEQ ID NO:1 (claim 15), wherein said antibody is detectably labeled (claim 16).

Sodhi, et al teach the use of anti-phosphotyrosine-FITC antibody, a fluorescently labeled and detectable antibody, to study proteins. It is an inherent property of the prior art antibody to specifically bind tyrosine phosphorylated proteins. In light of the specification, it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds PSTPIP. Therefore, the prior art antibody clearly anticipates the claims since the antibody is known to be capable of specifically binding a polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1. Moreover, the prior art antibody clearly anticipates a detectably labeled antibody capable of specific binding to PSTPIP since, in light of the specification, fluorescein isothiocyanate (FITC) is preferably used as a detectable label.

All the limitations of the claims are met.

17. Claims 15 and 17-18 would still be rejected under 35 U.S.C. 102(b) as being anticipated by Frackleton, et al (*Journal of Biological Chemistry*, 1984, **259**: 7909-7915; see abstract).

Claims 15 and 17-18 are drawn to an antibody capable of specifically binding a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 (claim 15) and a hybridoma cell line producing said antibody (claim 18), wherein the said antibody is a monoclonal antibody (claim 17).

Frackleton, et al teach the use of a monoclonal anti-phosphotyrosine antibody to isolate proteins. It is an inherent property of the prior art antibody to specifically bind tyrosine phosphorylated proteins. In light of the specification, it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds PSTPIP. Therefore, the prior art antibody clearly anticipates the claims since the antibody is known to be capable of specifically binding a polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1. In light of the specification and the art at the time of the invention, inherent in the production of a monoclonal antibody is the hybridoma cell line that produces a monoclonal antibody.

All the limitations of the claims are met.

18. Claims 15 and 17 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Su, et al (*Biotechniques* **13**: 756-762, 1992).

Claims 15 and 17 are drawn to an antibody capable of specifically binding a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 (claim 15), wherein the antibody is a monoclonal antibody (claim 17).

Su, et al taught the use of an anti-FLAG monoclonal antibody for immunoaffinity chromatography and Western protein analysis.

It is an inherent property of the prior art antibody to specifically bind fusion proteins comprising a PSTPIP polypeptide fused with a FLAG epitope tag. In light of the specification, it is clear that an anti-FLAG monoclonal antibody specifically binds FLAG-tagged PSTPIP. Therefore, the prior art antibody clearly anticipates the claims since said antibody is known to be capable of specifically binding a polypeptide comprising the

amino acid sequence indicated by SEQ ID NO:1. In light of the specification and the art at the time of the invention, inherent in the production of a monoclonal antibody is the hybridoma cell line that produces a monoclonal antibody.

Su, et al anticipated a monoclonal antibody capable of specifically binding to a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 and a hybridoma cell line which produces said monoclonal antibody. All the limitations of the claims are met.

In order to overcome this rejection, the examiner suggests that claim could be amended to read "an antibody capable of specific binding to an epitope of the polypeptide consisting of the amino acid sequence indicated by SEQ ID NO:1".

19. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Parthun, et al (*Journal of Biological Chemistry*, 1990, 265: 209-213).

Claim 15 is drawn to an antibody capable of specifically binding a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1.

Parthun, et al taught the use of an antibody for analysis of yeast GAL4 transactivating protein. Parthun, et al disclosed that "the 881-amino acid GAL4 protein has been examined extensively through in vivo analysis of deletion constructs and the use of in vitro translation products" (page 209, spanning columns 1 and 2). Also, Parthun, et al disclosed that "anti-GAL4 antisera was generously provided by S. Johnston (Duke University)" (page 210, second column). S. Johnston and coworkers disclosed the

sequence of the isolated gene encoding GAL4 (see *Proceedings of the National Academy of Science USA* **79**: 6971-6975, 1982). A Geneseq Data Bank search (US-09-068-377-2.rng; result 3) revealed that the polynucleotide indicated by SEQ ID NO:2, which encodes the PSTPIP polypeptide comprising SEQ ID NO:1, is 100% identical over a span of 344 nucleotides to the sequence of a nucleic acid molecule encoding GAL4 transactivating protein (see US-09-068-377-2.rng, results 3).

It is an inherent property of the prior art antibody to recognize an inherent feature in the structure of a protein determined by its amino acid sequence and to specifically that feature, commonly referred to as an epitope. It is clear that the GAL4 gene encodes a protein that is identical in amino acid sequence to at least a portion of the amino acid sequence comprising SEQ ID NO:1. The prior art antibody anticipates the claims since said antibody will be capable of specifically binding a polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 upon recognition of commonly displayed antigenic epitopes.

Parthun, et al anticipated an antibody capable of specifically binding to a polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1. All the limitations of the claims are met.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett, et al (Geneseq accession no. T43136; CA2150039-A, 1996) or Geneseq Data Bank search result 3 (US-09-068-377-2.rng), in view of US 5,001,225-A.

Claim 15 is drawn to an antibody capable of specifically binding a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 or capable of specific binding to a polypeptide encoded by a nucleic acid molecule hybridizing to the complement of SEQ ID NO:2 under specifically claimed stringent conditions, said polypeptide having a substantially retained the ability to bind a protein tyrosine phosphatase which has specifically claimed properties. Claim 16 is drawn to the antibody of claim 15 that is detectably labeled.

It is noted that for the purposes of examination, in view of the use of indefinite claim language, for the reasons set forth above, claim 15 is interpreted to encompass a genus of polypeptides with a ranging retention of ability to bind a protein tyrosine phosphatase (PTP), wherein the ability retained by said polypeptides ranges from no retention to full retention of the ability to bind PTP.

Bennett, et al disclose the sequence of a polynucleotide having 100% identity with the nucleic acid molecule indicated by SEQ ID NO:2 that encodes the PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 over a range of 344 nucleotides (see Geneseq Data Bank search result 3). Bennett, et al taught that the polynucleotide sequence encodes Gal4 transactivating protein.

Bennett, et al did not expressly disclose an antibody capable of specific binding to the Gal4 transactivating protein encoded by the polynucleotide sequence. Bennett, et al did not expressly disclose said antibody that is detectably labeled.

US 5,001,225 (1991) teaches that alkaline phosphatase can be added to monoclonal antibody 7H8 to facilitate determination of the presence or amount of plasmodium-associated antigen in a sample.

The complement of the nucleic acid molecule comprising SEQ ID NO:2 would be expected to hybridize to the polynucleotide encoding the Gal4 transactivating protein under the specifically claimed stringent conditions. Nucleic acid molecules with identical polynucleotide sequences will encode polypeptides with identical amino acid sequences translated from the same open reading frame. Given the polynucleotide sequence, one of ordinary skill in the art would instantly envision the encoded polypeptide.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention to make a polyclonal antibody to the encoded polypeptide because the Board of Patent Appeals and Interferences has taken the position that once an antigen has been isolated, the manufacture of monoclonal antibodies against the antigen is *prima facie* obvious (see Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Board of Patent Appeals and Interferences), 1987; Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Board of Patent Appeals and Interferences), 1990). One would expect that a subset of these antibodies would bind the polypeptide comprising the amino acid

sequence indicated by SEQ ID NO:1 with a reasonable expectation of success.

Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention was made to conjugate the antibody to a detectable label, such as horse radish peroxidase (HRP) or alkaline phosphatase, because US 5,001,225-A teaches that adding a label to an antibody provides a method of determining the presence or amount of an antigen in a sample (see column 6, lines 45-68).

One of ordinary skill in the art would have been motivated to detectably label the antibody because antibodies to the Gal4 transactivating protein are a valuable reagent that could be used in order to easily detect the Gal4 transactivating protein on a blot during Western protein analysis.

22. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Green Cross Corp. (Geneseq accession no. Q61607; JO6078767-A, 1994) and Geneseq Data Bank search result 6 (US-09-068-377-2.rng).

Claim 15 is drawn to an antibody capable of specifically binding a PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 or capable of specific binding to a polypeptide encoded by a nucleic acid molecule hybridizing to the complement of SEQ ID NO:2 under specifically claimed stringent conditions, said polypeptide having a substantially retained the ability to bind a protein tyrosine phosphatase which has specifically claimed properties. The claim encompasses any

antibody, including a polyclonal or a monoclonal antibody, capable of specific binding to a PSTPIP-like polypeptide.

Further, it is noted that for the purposes of examination, in view of the use of indefinite claim language, for the reasons set forth above, claim 15 is interpreted to encompass a genus of polypeptides with a ranging retention of ability to bind a protein tyrosine phosphatase (PTP), wherein the ability retained by said polypeptides ranges from no retention to full retention of the ability to bind PTP.

JO6078767-A discloses the sequence of a polynucleotide having 100% identity with the nucleic acid molecule indicated by SEQ ID NO:2 that encodes the PSTPIP polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 over a range of 280 nucleotides (see Geneseq Data Bank search result 6). The reference teaches that this polynucleotide encodes a mutated GAL4 transcriptional activator.

JO6078767-A did not expressly disclose an antibody capable of specific binding to the Gal4 transactivating protein encoded by the polynucleotide sequence.

The complement of the nucleic acid molecule comprising SEQ ID NO:2 would be expected to hybridize to the polynucleotide encoding the Gal4 transactivating protein under the specifically claimed stringent conditions. Nucleic acid molecules with identical polynucleotide sequences will encode polypeptides with identical amino acid sequences translated from the same open reading frame. Given the polynucleotide sequence, one of ordinary skill in the art would instantly envision the encoded polypeptide.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because the Board of Patent Appeals and Interferences has taken the position that once an antigen has been isolated, the manufacture of monoclonal antibodies against the antigen is *prima facie* obvious (see Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Board of Patent Appeals and Interferences), 1987; Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Board of Patent Appeals and Interferences), 1990). One would expect that a subset of these antibodies would bind the polypeptide comprising the amino acid sequence indicated by SEQ ID NO:1 with a reasonable expectation of success.

Conclusion

23. No claims are allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner, Art Unit 1642

slr
November 2, 2000

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

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PRIMARY EXAMINER